Table 14: **Env**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Env( )	gp120( )		Vaccine	murine( )	[Shiver1997b]
Vaccine: *Vector/type:* DNA *Strain:* IIIB *HIV component:* gp120, gp160					
• DNA vaccinations of BALBc mice with a gp120 or gp160 DNA vaccine elicited a strong T-cell proliferative response with Th1-like secretion of γ interferon and IL-2, with little or no IL-4, as well as antigen specific gp120 Abs • An intramuscular route of inoculation gave a stronger proliferative response than intradermal • A proliferative response could be detected in all lymph tissues tested: spleen, PBMC, and mesenteric, iliac, and inguinal lymph nodes					
Env( )	gp120( )		Vaccine	murine( )	[Kim1997f]
Vaccine: *Vector/type:* DNA *HIV component:* gp160, Gag, Pol *Stimulatory Agents:* CD86 expression vector					
• A gp160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecule CD86, gives an increase in the proliferative responses to gp120 in mice					
Env( )	gp120( )			human( )	[DeBerardinis1997]
• Sequences flanking helper T-cell immunogenic domains can be important for immunogenicity					
Env( )	gp120( )	polyclonal	HIV-1 infection	human( )	[Rosenberg1997]
• A strong proliferative response to p24 and gp160 was found in a healthy long term survivor					
Env( )	gp120( )	polyclonal	HIV-1 infection	Macaca nemestrina( )	[Kent1997c]
• Macaca nemestrina can be infected with HIV, and clear the infection within 6 months, so it is of interest to examine their initial immune response • A strong proliferative response against gp160 with IL-4 production, indicating a Th2 response, was found with 4 weeks of infection • The gp160 proliferative response by 8 weeks produces both IL-4 and γ interferon, indicating both Th1 and Th2 responses					
Env( )	gp120( )	polyclonal	Vaccine	Rhesus macaque( )	[Letvin1997b]
Vaccine: *Vector/type:* DNA prime with rgp160 boost *Strain:* HXBc2 *HIV component:* gp160					
• Vaccination of Macaca mulatta (rhesus monkeys) with a HXBc2 env DNA prime and a protein boost elicited a T-cell proliferative response, a CTL response, and type-specific neutralizing antibodies • Vaccinated animals challenged with SHIV-HXB2 were protected from infection					
Env( )	gp120( )	polyclonal	HIV-1 infection, Vaccine	human( )	[MacGregor1998b]
Vaccine: *Vector/type:* DNA *Strain:* MN *HIV component:* Env, Rev					
• An HIV DNA env and rev vaccine given to 15 asymptomatic HIV+ individuals at three different dosages, 30, 100 or 300 μg, was safe • All three groups showed an increased proliferative response after vaccination					

Env( )	Env( )	HIV-1 exposed seronegative	human( )	[Mazzoli1997]

- Study of HIV-specific immunity in seronegative partners of HIV-positive individuals – Env peptides could stimulate IL-2 production in 9/16 HIV-exposed seronegative individuals, and only 1/50 low-risk controls
- Exposed-uninfected produced more IL-2 and less IL-10 than HIV-infected individuals
- 8/9 of those whose PBMC produce IL-2 in response to Env peptides had concomitantly detected urinary or vaginal tract anti-HIV IgA

Env( )	Env( )	HIV-1 infection	human( )	[Plana1998]

- Patients from later stages of infection given HAART do not show restoration of HIV-1 specific Th proliferative responses

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Env( )	Env( )	HIV-1 infection	human( )	[Kelleher1998a]

- Env and gag Th epitopes were pooled and used to test Th proliferative responses after IL-2 therapy – while IL-2 therapy causes an increase in CD4+ lymphocyte count, it does not increase HIV-1 specific proliferative responses

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Env( )	gp160( )	HIV-1 infection, Vaccine	human( )	[Ratto-Kim1999]

Vaccine: *Vector/type:* recombinant protein *HIV component:* gp160

- Vaccinations with rgp160 did not enhance Th immunoproliferative responses in individuals who were immunized every 2 months for 5 years starting early in infection

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Env( )	gp160( )	HIV-1 infection, Vaccine	human( )	[Leandersson2000]

Vaccine: *Vector/type:* recombinant protein *HIV component:* gp160

- 27 HIV subtype B, 4 subtype C, 2 D and one of each subtype E, F, G were either given rgp160 B clade immunizations or placebo – all rgp160 immunized individuals showed increased proliferation responses to the B clade immunizing antigen rgp160
- gp120 was prepared from A, B, C, D, and E subtype virions and used as antigenic stimulus – 7 of 10 tested individuals responded to native gp120 from at least one additional subtype in addition to B subtype, while a placebo recipient did not respond to any gp120
- This study shows that cross-subtype HIV-specific T-cell proliferative responses can be stimulated in patients already infected with another HIV-1 subtype – all immunized subjects could respond to the subtype B immunogen, but many developed responses to at least one more subtype

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Env( )	gp160( )	Vaccine	human( )	[Gorse1999a]

Vaccine: *Vector/type:* gp160 prime with gp120 boost *Strain:* MN *HIV component:* gp160, gp120

- Helper T-cell memory responses were induced by MN rgp160 as measured by proliferation and Th1 and Th2 cytokine release – this response could be boosted by MN rgp120

Env( )	gp120( )	Vaccine	Rhesus macaque( )	[Heeney1998]

Vaccine: *Vector/type:* ISCOM or fowlpoxvirus *Strain:* SF2 *HIV component:* gp120

- Vaccinated monkeys with the highest level of Th1 and Th2 responses and the highest levels of NAbs were protected against a SHIV SF13 challenge – the ISCOM strategy gave more potent anti -gp120 responses than the Fowl pox strategy
- When animals were challenged 4 months after boost, those that maintained high levels of HIV-1 specific IFN-γ responses, indicative of a Th1 response, were still protected

Env( )	( )	HIV-1 infection, Vaccine	human( )	[Boyer1999]

Vaccine: *Vector/type:* DNA *Strain:* IIIB *HIV component:* Env, Rev

- A DNA vaccine containing env and rev was tested for safety and immune response in 15 HIV+ asymptomatic individuals
- Enhanced proliferative activity and higher levels of MIP-1α were detected in multiple study subjects

Env( )	Env( )	Vaccine	murine BALB/c( )	[Rodriguez1999]

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* gp160 *Stimulatory Agents:* GM-CSF-Env chimera

- A chimeric GM-CSF-Env antigen expressed in a vaccinia vector elicits a higher HIV-specific Env cellular immune response than when native Env is used

Env( )	Env( )	Vaccine	Macaca nemestrina( )	[Kent1998a]

Vaccine: *Vector/type:* DNA prime with vaccinia boost *Strain:* LAI *HIV component:* Env, Gag

- Priming with an HIV-DNA vaccine and boosting with a vaccinia construct induced greater levels of HIV T-cell immunity than either vaccine alone
- The proliferative response to Env and Gag after the DNA vaccination had a mean SI of 1.5-4, but after boosting with rHIV-fowlpox virus, there was a 6-17 fold increase in the mean SI for HIV Gag and Env. The T-helper response happened despite a fall in antibody titers, suggesting that the Th response was primarily Th1, not Th2. The CTL response was also enhanced

Env( )	gp120( )	Vaccine	Rhesus macaque( )	[Heeney1999b]

Vaccine: *Vector/type:* DNA, protein, virus-like particle, ISCOM

- Ten different vaccine strategies were evaluated for their ability to protect from infection in a rhesus macaque model using a non-pathogenic SHIV challenge. Protection correlated with the magnitude of NAb responses, β-chemokines, and a balanced Th response. DNA, protein+adjuvant, VLP and ISCOM vaccines were tested.
- HIV-1/ISCOMS gave the highest NAb titers, Th1 and Th2 responses, was the only vaccine formulation tested with a detectable CTL response, and gave enhanced β-chemokine production

Env( )	gp160( )	HIV-1 infection, Vaccine	human( )	[Kundu1998c]

Vaccine: *Vector/type:* protein *Strain:* MN *HIV component:* gp160

- This study followed 10 HLA-A2 asymptomatic HIV+ individuals as they received MN gp160 vaccinations over a two year period.
- There was an increased lymphoproliferative response but this did not impact viral load or CTL response

Env( )	gp120( )	Vaccine	Rhesus macaque( )	[Verschoor1999]

Vaccine: *Vector/type:* DNA, recombinant protein, ISCOM *Strain:* SF2 *HIV component:* gp120 *Stimulatory Agents:* Adjuvant MF59

- 16 rhesus Macaques were vaccinated with either an epidermal SF2 gp120 DNA vaccine, rgp120 with a MF59 adjuvant, or rgp120 incorporated into ISCOMs

- DNA vaccination elicited a weak Th type 1 response and low antibody response, rgp120/MF59 triggered a strong antibody response, and rgp120/ISCOM induced both kinds of Th cells, and a strong humoral response.
- Animals were challenged with SF13 SHIV. Early induction of Th type 1 and type 2 responses with the rgp120/ISCOM vaccine provided the most effective immunity, protecting from infection

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Env( ) Env( ) Vaccine murine( ) [Kim1998d]

Vaccine: *Vector/type:* DNA *Strain:* MN *HIV component:* Gag, Pol, Env *Stimulatory Agents:* CD80 and CD86 expression vectors

- Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses

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Env( ) Env( ) Vaccine human( ) [Salmon-Ceron1999a]

Vaccine: *Vector/type:* canarypox *Strain:* MN, LAI *HIV component:* gp120, gp41, Gag, Protease

- A live attenuated canarypox vector expressing MN gp120 and LAI gp41/gag/protease could induce CTL and a lymphoproliferative response in healthy uninfected volunteers

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Env( ) Env( ) Vaccine Rhesus macaque( ) [Akahata2000]

Vaccine: *Vector/type:* DNA *Strain:* ZF1 *HIV component:* complete genome

- Rhesus macaques were vaccinated by i.m. injection with naked plasmid DNA carrying an HIV-1 complete genome vaccine, strain ZF1, with a mutated zinc finger in the nucleocapsid to prevent packaging
- Env and Gag specific CTL but no antibody responses were induced in 2/4 vaccinated monkeys (MM145 and MM153)
- 2/4 monkeys (MM146 and MM143) produced antibodies against p24 and/or gp160, but no CTL response was detected
- PBMC from all vaccinated monkeys produced IFNγ, in response to HIV-1 gp160, indicating a Th response – this response was 5 times higher in MM145, the animal with the strongest CTL response
- 4 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM145 and MM153 (with a homologous Env) decreased to near or below the detection limit
- 6-8 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM146 and MM143 decreased near or below the detection limit

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Env( ) gp120( ) HIV-1 infection human( ) [Zhang2001]

- T-helper cell proliferative responses to HIV p24, p55 and gp120 were tested in 27 patients with HIV infection – vigorous responses directed at Gag were detected in ten patients, but an Env specific response was detected in only one patient

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Env( ) gp160( ) HIV-1 infection human( ) [Blazevic2000]

- Prolonged viral suppression resulting from potent anti-retroviral therapy did not allow an HIV T-helper response increase to p24 or gp160, but Th proliferative responses to influenza, alloantigen, and PHA did develop in many HIV+ patients, and asymptomatic patients had stronger and more frequent Th response recovery than AIDS patients

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Env( ) gp120( ) HIV-1 infection human( ) [Oxenius2000b]

- Patients who started therapy at acute HIV infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable

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Env( ) gp120( ) Vaccine human( ) [Sabbaj2000]

Vaccine: *Vector/type:* canarypox prime with rgp120 boost *HIV component:* gp120

- Proliferative responses in PBMC of uninfected individuals that were vaccinated with canarypox vector expressing HIV-1 antigens (ALVAC-HIV) and boosted with a recombinant gp120 subunit vaccine gave a Th1 and Th2 proliferative response upon stimulation with HIV-1 Env
- All vaccinees produced IFNγ and IL110, most also produced IL-2, IL-6, IL-4 and IL-5

Env( ) gp120( ) Vaccine murine(H-2^d) [Kim2000a]

Vaccine: *Vector/type:* DNA *HIV component:* Gag, Pol, Env *Stimulatory Agents:* IL-2, IL-4 and IFNγ expression vectors

- Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of Th1 cytokine IFN-γ drove Th1 immune responses and enhanced CTL responses

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Env( ) gp120( ) Vaccine murine(H-2^d) [Shirai2001]

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* gp160

- Helicobacter pylori induces Th1 responses early, but predominantly Th2 responses later in infection (at 6 weeks) – differentiation of HIV-1 gp160 CD4+ help and CD8+ CTL effector cells in response to HIV gp160-vaccinia vaccination is impaired in BALB/c mice infected with H. pylori

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Env( ) gp160( ) Vaccine murine(H2^d) [Morris2000a]

Vaccine: *Vector/type:* peptide, recombinant protein *Strain:* IIIB *HIV component:* gp160, V3 *Stimulatory Agents:* Adjuvant LT(R192G)

- Mice were intranasally immunized with 20 ug of HIV-gp160 and 5 ug of peptide E7 (RIHIGPGRAFYAARK) with the adjuvant LT(R192G), a heat-labile enterotoxin produced by *E. coli*
- Adjuvant LT(R192G) was required for stimulation of antigen-specific IgG1, IgG2 antibodies, and Th1 and Th2 cytokines responses to gp160, and peptide-specific CTL responses
- Increased IFN-γ, IL-10 and IL-6 cytokine production specific to gp160 was measured with co-immunization of gp160 with LT(R192G)

Env( ) gp160( ) Vaccine murine(H2^d) [Arai2000a]

Vaccine: *Vector/type:* DNA, CMV promotor *Strain:* IIIB *HIV component:* gp160, Rev *Stimulatory Agents:* Br-cAMP

- The CMV promotor responds to the intracellular level of cAMP, and 8 Br-cAMP can increase transgene expression so it was co-administered with a CMV-based DNA vaccine both intranasally and intramuscularly
- 8 Br-cAMP increased serum IgG responses, HIV-specific CTL, DTH and Th1 responses, and IgA in the intranasal vaccination
- A CAT assay study showed adjuvant effect was due to CMV promotor activation

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